

<https://helda.helsinki.fi>

Insomnia symptoms increase during pregnancy, but no increase in sleepiness - Associations with symptoms of depression and anxiety

Aukia, Linda

2020-08

Aukia , L , Paavonen , E J , Jänkälä , T , Tolvanen , M , Korja , R , Karlsson , L , Karlsson , H & Polo-Kantola , P 2020 , ' Insomnia symptoms increase during pregnancy, but no increase in sleepiness - Associations with symptoms of depression and anxiety ' , Sleep Medicine , vol. 72 , pp. 150-156 . <https://doi.org/10.1016/j.sleep.2020.03.031>

<http://hdl.handle.net/10138/328852>

<https://doi.org/10.1016/j.sleep.2020.03.031>

cc_by_nc_nd

acceptedVersion

Downloaded from Helda, University of Helsinki institutional repository.

This is an electronic reprint of the original article.

This reprint may differ from the original in pagination and typographic detail.

Please cite the original version.

Journal Pre-proof

Insomnia symptoms increase during pregnancy, but no increase in sleepiness -
Associations with symptoms of depression and anxiety

Linda Aukia, MD, E. Juulia Paavonen, MD, PhD, Tuire Jänkälä, MSc, Mimmi Tolvanen, PhD, Riikka Korja, PhD, Linnea Karlsson, MD, PhD, Hasse Karlsson, MD, PhD, Päivi Polo-Kantola, MD, PhD

PII: S1389-9457(20)30152-0

DOI: <https://doi.org/10.1016/j.sleep.2020.03.031>

Reference: SLEEP 4378

To appear in: *Sleep Medicine*

Received Date: 11 November 2019

Revised Date: 26 February 2020

Accepted Date: 26 March 2020

Please cite this article as: Aukia L, Paavonen EJ, Jänkälä T, Tolvanen M, Korja R, Karlsson L, Karlsson H, Polo-Kantola P, Insomnia symptoms increase during pregnancy, but no increase in sleepiness - Associations with symptoms of depression and anxiety, *Sleep Medicine*, <https://doi.org/10.1016/j.sleep.2020.03.031>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier B.V.



Insomnia symptoms increase during pregnancy, but no increase in sleepiness - Associations with symptoms of depression and anxiety

Linda Aukia, MD^{1¥}, E. Juulia Paavonen MD, PhD^{2,3}, Tuire Jänkälä, MSc^{4,5}, Mimmi Tolvanen, PhD⁴, Riikka Korja, PhD^{4,5}, Linnea Karlsson, MD, PhD^{4,6,7}, Hasse Karlsson, MD, PhD^{4,7,8} and Päivi Polo-Kantola, MD, PhD^{1,9}

1 Department of Obstetrics and Gynecology, Turku University Hospital and University of Turku, Turku, Finland

2 Pediatric Research Center, Child Psychiatry, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

3 National Institute for Health and Welfare, Helsinki, Finland

4 FinnBrain Birth Cohort Study, Turku Brain and Mind Center, Institute of Clinical Medicine, University of Turku, Turku, Finland

5 Department of Psychology, University of Turku, Turku, Finland

6 Department of Child Psychiatry, Turku University Hospital and University of Turku, Turku, Finland

7 Centre for Population Health Research, Turku University Hospital and University of Turku

8 Department of Psychiatry, Turku University Hospital and University of Turku, Turku, Finland

9 Sleep Research Unit, Department of Physiology, University of Turku, Turku, Finland

¥Corresponding author:

Linda Aukia

Department of Obstetrics and Gynecology, Turku University Hospital and University of Turku

Kiinamylynkatu 4-8

20520 Turku, Finland

email: lelink@utu.fi

tel:+358 40 5693404

Contributions: Linda Aukia (ORCID iD 0000-0003-1930-2984) is the principal investigator and writer of the paper and co-leader of the present sub-study. Tuire Jänkälä (ORCID iD 0000-0003-0580-1213), Mimmi Tolvanen, Riikka Korja (ORCID iD 0000-0002-6833-1565) and Linnea Karlsson (ORCID iD 0000-0002-4725-0176) are co-investigators and co-writers. Hasse Karlsson (ORCID iD 0000-0002-4992-1893) is the leader of the FinnBrain study, co-investigator and co-writer. E.Juulia Paavonen (ORCID iD 0000-0002-1421-9877) and Päivi Polo-Kantola (ORCID iD 0000-0003-0665-0306) are co-leaders of the present sub-study, co-investigators and co-writers.

Abstract

Objective: To evaluate alteration in insomnia and sleepiness symptoms during pregnancy and assess early pregnancy risk factors for these symptoms, especially depressive and anxiety symptoms.

Methods: A cohort of 1858 women was enrolled from the FinnBrain Birth Cohort Study. Insomnia and sleepiness symptoms were measured in early, mid- and late pregnancy with the Basic Nordic Sleep Questionnaire. Depressive symptoms were measured using the Edinburgh Postnatal Depression Scale and anxiety symptoms with the Symptom Checklist-90/Anxiety Scale. General linear models for repeated measures were conducted.

Results: General sleep quality decreased ($p < 0.001$) and all insomnia types ($p < 0.001$) and sleep latencies ($p < 0.001$) increased as pregnancy proceeded. Snoring increased, but witnessed apneas remained rare. Nevertheless, morning ($p = 0.019$) and daytime ($p < 0.001$) sleepiness decreased from early to both mid-pregnancy and late pregnancy ($p = 0.006$ and $p = 0.039$). Women took more naps in early and late pregnancy compared to mid-pregnancy (both $p < 0.001$). Women with higher baseline anxiety symptoms had greater increase in sleep latency. At each pregnancy point, higher depressive and anxiety symptoms were associated with higher insomnia ($p < 0.001$) and sleepiness scores ($p < 0.001$) and higher depressive symptoms with longer sleep latencies ($p < 0.001$).

Conclusion: We found a marked increase in insomnia symptoms throughout pregnancy. However, sleepiness symptoms did not increase correspondingly. Both depressive and anxiety symptoms in early pregnancy were associated with higher insomnia and sleepiness symptoms in later stages of pregnancy which emphasizes the importance of their assessment in early pregnancy.

Key Words: Sleep disturbance; insomnia; nocturnal breathing problems; sleepiness; pregnancy; depression; anxiety

1. Introduction

Sleep quality during pregnancy is important, as previous literature proposes an association between sleep disturbances and adverse pregnancy and delivery outcomes [1–3]. Mainly cross-sectional [4–9], but also a few longitudinal studies show [10–13] that sleep quality deteriorates throughout pregnancy. However, the prevalence of different sleep disturbances during pregnancy still remains unclear, as most of the previous studies have been cross-sectional, or small. Only one study has previously reported the prevalence rates of different insomnia symptoms throughout pregnancy [12].

Nocturnal breathing problems, especially snoring, are common during pregnancy [4–6,14]. Although nocturnal breathing problems have been shown to relate with pregnancy complications [3], previous literature describing the course of the frequency of these symptoms is sparse, suggesting an increase as pregnancy proceeds [6,15]. Further, some studies have shown that obstructive sleep apnea (OSA) is more common in pregnant than in non-pregnant women [16], especially in overweight [15,17,18] or older [18] women.

Some concerns of sleep disturbances are the daytime consequences, like sleepiness, lower vigilance, or cognitive problems [19], as well as the effects of sleep disturbances on physical and mental health [20–22]. Although a higher prevalence of sleep disturbances in late pregnancy has quite unanimously been reported, previous studies about alterations in sleepiness are sparse with inconsistent findings. One study found a persistently high sleepiness throughout pregnancy [5], whereas another study

showed that sleepiness was the most frequent in early pregnancy, subsequently diminishing later [6]. Two more studies, however, proposed a U-shape occurrence of sleepiness with the lowest occurrence in mid-pregnancy [12,23].

Mood symptoms are common during pregnancy [24–26]. Among the general population, mood symptoms and sleep disturbances are strongly related [27].

Similarly, pregnant women with mood symptoms suffer from insomnia [28–32] and decreased sleep efficiency [28]. However, the associations are bi-directional; insomnia can increase the severity of depressive symptoms, but also depression itself can worsen sleep quality. During pregnancy, the associations remain controversial. In one previous study, poor general sleep quality in early pregnancy predicted higher levels of depression in later pregnancy, but not vice versa [33]. In another study, both cross-sectional and longitudinal associations between sleep and depressive and anxiety symptoms were found [34].

Thus, we conducted a prospective study with a representative number of women to study the prevalence of sleep disturbances during the three trimesters of pregnancy.

We hypothesized that insomnia and sleepiness symptoms, as well as nocturnal breathing problems, increase as pregnancy proceeds. In addition, we explored early risk factors for sleep disturbances, and hypothesized that especially depressive and anxiety symptoms in the first trimester predict worsening in sleep quality.

2. Materials and methods

The present study was a part of the longitudinal FinnBrain Birth Cohort Study conducted at the University of Turku, Finland (www.finnbrain.fi). In the FinnBrain Birth Cohort Study, the women and their offspring are followed starting from the

prenatal period until the adulthood of the children. The pregnant women were recruited between December 2011 and April 2015 from Turku and Åland hospital districts at their routine ultrasound appointment at around gestational week (gw) 11 by trained research nurses. After oral and written information, the women who gave their written consent were eligible for the study. STROBE guidelines [35] were followed in the research and reporting of this study.

To obtain information on sleep quality, the questionnaires were sent at around gw 14 (early pregnancy point), gw 24 (mid-pregnancy point) and gw 34 (late pregnancy point). Responses given between 11+2–16+6 gwks (mean 14+6, SD 0.85; early pregnancy), between 22+0–27+6 gwks (mean 25+0, SD 1.01; mid-pregnancy) and between 32+0–38+0 (mean 35+1, SD 0.91; late pregnancy) were accepted into the study. The questionnaires were sent to the women either by post or by e-mail. If no response was received within two weeks, two reminders were sent by text message in the 3rd and 4th week after the original questionnaire.

Together with the first questionnaire, at gw 14, another questionnaire concerning background information was sent to the women. The questions included information of age (years), body mass index (BMI kg/m²), marital status (married/cohabited/divorced/single), parity (nulliparous/multiparous [number of children]), education (low/middle/high) and smoking (yes/no).

The FinnBrain cohort consisted of 3808 women, of which 3242 women completed and returned at least one of the questionnaires during pregnancy. A total of 1858 women completed and returned all three questionnaires within the acceptable time window and were thus eligible for this study, giving the response rate of 57.3% (Fig. 1). The characteristics of the women are described in Table 1.

Sleep quality over the previous month was evaluated with the Basic Nordic Sleep Questionnaire (BNSQ) [37]. Of the original BNSQ questionnaire, 11 questions were used in this study. General sleep quality was rated with on 5-point scale as 'good', 'quite good', 'intermediate [neither good nor poor]', 'quite poor' or 'poor'. Insomnia symptoms included difficulty falling asleep, nocturnal awakenings per week, frequency of nocturnal awakenings per night and waking up too early in the morning without the ability to go back to sleep. Nocturnal breathing problems included snoring and witnessed apneas, and women were encouraged to ask their spouse/other persons nearby if they had observed these symptoms. Sleepiness symptoms included sleepiness in the morning, sleepiness in the daytime and napping during the day. These questions were rated on a 5-point scale with the following response alternatives: 1 = 'never or less than once a month', 2 = 'less than once a week', 3 = 'once or twice a week', 4 = 'three to five times a week' and 5 = 'daily or almost daily', and in the question regarding frequency of nocturnal awakenings per night 1 = 'none', 2 = 'once', 3 = 'twice', 4 = 'three to four times', 5 = 'at least five times'. The 5-point sleep variables (general sleep quality, difficulty falling asleep, nocturnal awakenings per week, frequency of nocturnal awakenings per night, waking up too early in the morning, snoring, apneas, sleepiness in the morning, sleepiness in the daytime and napping) were dichotomized: in responses '1' to '3' the sleep disturbance occurred \leq two times/week and in responses '4' to '5' \geq three times/week in order to differentiate the severity of the sleep disturbances according to the frequencies [38].

The insomnia score was calculated as a sum score of the five questions: general sleep quality, difficulties in falling asleep, nocturnal awakenings (two separate questions: both weekly and nightly) and too early morning awakenings. The

sleepiness score was a sum score of three questions: morning sleepiness, daytime sleepiness and daytime naps. When creating the total scores, missing answers were substituted with the mean value of the same woman's answers. The Cronbach's alpha for the insomnia score was 0.689–0.722, and for the sleepiness score 0.581–0.697 at different time points. In addition, sleep latency (minutes) was assessed separately for workdays and for leisure days and an average latency was calculated accordingly.

The Edinburgh Postnatal Depression Scale (EPDS) [39,40] was used to measure depressive symptoms in early pregnancy. The EPDS is a widely used and well validated self-report questionnaire validated for rating depression in the prenatal period as well [39,40]. The EPDS consists of 10 questions, and answers are given on a 4-point scale, with values between 0–3 for each item, and thus, the sum score ranges from 0 to 30. A higher score indicates higher depressive symptoms. Cronbach's alpha for the EPDS score at baseline was 0.815.

Anxiety was assessed using a validated Symptom Checklist -90/Anxiety Scale (SCL-90/anxiety scale) [41,42]. The scale consists of 10 questions and the answers are given on a 5-point Likert scale ranging from 'not at all' to 'extremely'. Each item is given a value between 0–4, and the sum score ranges from 0 to 40. A higher score indicates higher anxiety symptoms. Cronbach's alpha for the SCL-90 anxiety subscale at baseline was 0.832. The mean scores for depressive and anxiety symptoms at baseline are shown in Table 1.

Fig. 1 Flowchart of the study

Journal Pre-proof

Table 1 Characteristics of the women.

	n	Mean \pm SD or %	Range
Age (years)	1858	30.5 \pm 4.4	17–46
BMI (kg/m ²)	1826	24.6 \pm 4.7	16.6–57.8
Parity	1854		
Nulliparous		54%	
Multiparous		46%	
One previous child	604	72%	
Two previous children	187	22%	
Three or more previous children	55	6%	
Education	1855		
Low or middle level		34%	
High level		66%	
Marital status	1807		
Married/Cohabiting		98.7%	
Divorced		0.3%	
Single		1 %	
Smoking, early pregnancy	218	12%	
Depression score, early pregnancy	1854	5.0 \pm 4.0	0–27
Anxiety score, early pregnancy	1854	3.2 \pm 3.9	0–33

2.1. Statistical analysis

First, the prevalence of sleep disturbances with the mean and standard deviation (SD) was calculated separately at each time point. The differences in the prevalence of the dichotomized sleep variables across the three time points were studied using the McNemar test, while the differences in the continuous variables (insomnia and sleepiness score, sleep latency, EPDS, SCL-90) across the time points were studied using a Wilcoxon signed-rank test.

Next, a general linear model for repeated measures was calculated to evaluate how baseline depressive and anxiety symptoms were related to sleep quality during pregnancy. A multivariate model was calculated to predict the changes in sleep variables (sleep latency, insomnia score, sleepiness score) at each time point (early, mid- and late pregnancy). Depressive and anxiety symptoms were used as the main explanatory variables. In the modelling, these variables were used as continuous variables. The women's age, BMI, parity, education and smoking were included in the models as covariates. Statistical analyses were performed with IBM SPSS Statistics 25.

2.2. Ethical approval

The study has been approved by the Joint Ethics Committees of the University of Turku and Turku University Hospital, Turku, Finland (number ETMK 57/180/2011, meeting 14.6.2011 § 168).

3. Results

The drop-out analysis of this cohort, reported earlier [36], revealed some differences between the respondents and non-respondents: Older ($p = 0.005$) and nulliparous ($p = 0.005$) women were more likely to return the questionnaires at gwk 14 and at gwk 34. Women with higher education were more likely to return all of the questionnaires ($p < 0.001$) and women with fewer depressive symptoms at gwk 14 were more likely to return the questionnaires at gwk 34 ($p = 0.009$).

The prevalence of various sleep disturbances is illustrated on Table 2. General sleep quality had similar ratings during early and mid-pregnancy ($p = 0.106$), but the quality decreased in late pregnancy ($p < 0.001$ in both) (Table 2). All insomnia symptom types (difficulties falling asleep, number of nocturnal awakenings per week and per night, and too early morning awakenings) increased from early pregnancy to late pregnancy and from mid-pregnancy to late pregnancy (all $p < 0.001$). In addition, nocturnal awakenings per night increased from early pregnancy to mid-pregnancy ($p = 0.027$) (Table 2). The insomnia score increased as pregnancy proceeded: from early pregnancy to mid-pregnancy ($p < 0.001$) and from mid-pregnancy to late pregnancy ($p < 0.001$). Sleep latency also increased during pregnancy (all $p < 0.001$) (Table 3). Snoring increased throughout pregnancy but witnessed apneas remained rare (Table 2).

Morning and daytime sleepiness decreased from early to mid-pregnancy (morning sleepiness $p = 0.019$, daytime sleepiness $p < 0.001$), and also from early to late pregnancy (morning sleepiness $p = 0.006$, daytime sleepiness $p = 0.039$). In addition, morning sleepiness decreased from mid-pregnancy to late pregnancy ($p < 0.001$), whereas daytime sleepiness increased ($p = 0.005$). Furthermore, women took more naps in early and late pregnancy compared to mid-pregnancy ($p < 0.001$ in both)

and they took more naps in late pregnancy compared to early pregnancy ($p < 0.001$) (Table 2). The sleepiness score was highest in early pregnancy, and thereafter followed a U-shape: it decreased from early pregnancy to mid-pregnancy ($p < 0.001$) and increased from mid-pregnancy to late pregnancy ($p < 0.001$) (Table 3).

In the repeated-measures models, the relationship between baseline depressive and anxiety symptoms and changes in sleep quality during pregnancy was studied (within subjects effects), and women's age, BMI, parity, education and smoking were included as covariates. The women with more baseline anxiety symptoms had a greater increase in sleep latency compared to other women ($p = 0.012$). In addition, higher parity was associated with a higher increase in the total insomnia score ($p = 0.012$), and higher parity ($p < 0.001$) was related to an increase in the sleepiness score. The other covariates were not associated with sleep variables. (Table 4.)

The repeated-measures models also showed that the women with more baseline depressive and anxiety symptoms had higher levels of insomnia ($p < 0.001$ in both) and sleepiness scores ($p < 0.001$ in both) at each pregnancy point (between subject effects). In addition, those with more depressive symptoms had longer sleep latencies ($p < 0.001$). Women with lower education ($p = 0.029$) had longer sleep latencies throughout pregnancy. Furthermore, higher age ($p < 0.001$) was associated with a higher total insomnia and sleepiness scores during pregnancy and higher BMI ($p = 0.022$) were associated with a higher total insomnia. (Table 4.)

Table 2 Prevalence of sleep disturbances in early, mid- and late pregnancy.

	Total N	Early pregnancy ≥ 3/week or /night % (N)	Mid- pregnancy ≥ 3/week or /night % (N)	Late Pregnancy ≥ 3/week or /night % (N)	early vs mid <i>p</i>	mid vs late <i>p</i>	early vs late <i>p</i>
INSOMNIA							
Difficulty falling asleep per week	1846	5.4 % (100)	6.2% (114)	16.1% (299)	0.235	<0.001	<0.001
Nocturnal awakenings per week	1849	78.0% (1443)	76.8% (1420)	92.4% (1700)	0.236	<0.001	<0.001
Number of nocturnal awakenings per night	1844	12.6% (232)	14.4% (265)	34.8% (639)	0.027	<0.001	<0.001
Too early morning awakenings per week	1842	7,6% (140)	8,0% (148)	12,6% (231)	0.602	<0.001	<0.001
General sleep quality	1849	Poor ^a 13.3 (245)	Poor ^a 14.7 (271)	Poor ^a 30.2 (3556)	0.106	<0.001	<0.001
SLEEPINESS							
Morning sleepiness per week	1846	27.2% (502)	24.4% (451)	21.6% (397)	0.019	<0.001	0.006
Daytime sleepiness per week	1846	31.1% (574)	25.1% (464)	28.3% (521)	<0.001	0.005	0.039
Naps per week	1837	18.9% (348)	14.1% (259)	24.4% (446)	<0.001	<0.001	<0.001
NOCTURNAL BREATHING							
Snoring per week	1821	6.7% (122)	8.1% (148)	13.0% (236)	0.008	<0.001	<0.001
Witnessed apneas per week	1833	0.3% (5)	0.4% (7)	0.4% (7)	0.453	0.453	1.000

^aPoor or quite poor

Table 3 Symptoms of maternal insomnia, sleepiness and sleep latency in early, mid- and late pregnancy.

	n	Mean	95% CI for mean	SD	Range	early vs mid <i>p</i>	early vs late <i>p</i>	mid vs late <i>p</i>
Insomnia, early	1850	12.6	12.45–12.75	3.3	5–24	<0.001	<0.001	<0.001
Insomnia, mid	1850	12.9	12.71–13.01	3.3	5–24			
Insomnia, late	1841	15.1	14.93–15.24	3.4	5–25			
Sleepiness, early	1850	8.4	8.30–8.53	2.5	3–15	<0.001	<0.05	<0.001
Sleepiness, mid	1851	7.9	7.78–8.02	2.5	3–15			
Sleepiness, late	1843	8.3	8.15–8.41	2.7	3–15			
Sleep latency (min), early	1841	15.2	14.43–15.94	16.6	0–300	<0.001	<0.001	<0.001
Sleep latency (min), mid	1846	16.1	15.33–16.82	16.4	0–180			
Sleep latency (min), late	1823	21.0	19.93–22.02	19.7	0–300			

Table 4 Repeated-measures models between continuous sleep variables, basic characteristics, depressive and anxiety symptoms.

	β coefficients ¹	within subjects p-value (to indicate significant change over time)	between subjects p- value (to indicate significant difference across the timepoints)
Insomnia			
Age (years)	0.065, 0.069, 0.053	0.656	<0.001
BMI (kg/m ²)	0.032, 0.036, 0.027	0.844	0.022
Parity			
<i>Multipara vs. nullipara</i>	-0.540, -0.529, -0.144	0.012	0.003
Education		0.557	0.139
<i>Low vs. High</i>	0.192, 0.257, 0.481		
<i>Middle vs. High</i>	-0.004, -0.050, 0.145		
Smoking			
<i>Yes vs. no</i>	0.202, 0.208, 0.294	0.904	0.260
Depression score, points	0.180, 0.140, 0.148	0.218	<0.001
Anxiety score, points	0.107, 0.116, 0.106	0.904	<0.001
Sleep latency			
Age (years)	0.006, -0.152, -0.193	0.166	0.240
BMI (in kg/m ²)	-0.096, 0.126, 0.072	0.052	0.680
Parity			
<i>Multipara vs. nullipara</i>	1.053, 0.729, 0.476	0.812	0.349
Education		0.653	0.029
<i>Low vs. High</i>	2.875, 1.846, 3.086		
<i>Middle vs. High</i>	0.125, 0.240, 1.187		
Smoking			
<i>Yes vs. no</i>	0.895, -0.018, 0.217	0.794	0.771
Depression score, points	0.484, 0.617, 0.485	0.581	<0.001
Anxiety score, points	0.341, 0.121, 0.591	0.012	0.010
Sleepiness			
Age (years)	0.006, 0.031, 0.045	0.064	0.028
BMI (kg/m ²)	-0.002, 0.019, -0.010	0.054	0.811
Parity			
<i>Multipara vs. nullipara</i>	-0.013, -0.228, -0.644	<0.001	0.004
Education		0.320	0.837
<i>Low vs. High</i>	-0.035, -0.095, 0.175		
<i>Middle vs. High</i>	-0.087, -0.025, -0.055		
Smoking			

<i>Yes vs. No</i>	-0.005, -0.038, 0.211	0.471	0.602
Depression score, points	0.128, 0.140, 0.116	0.480	<0.001
Anxiety score, points	0.124, 0.079, 0.082	0.051	<0.001

¹ The presented coefficients are related to T1, T2, T3, respectively.

4. Discussion

We found that various insomnia symptoms were highly prevalent throughout pregnancy. In addition, all insomnia symptoms, as well as snoring, increased noticeably during pregnancy. Nevertheless, these disadvantageous changes in sleep disturbances were not reflected in an increase in morning or daytime sleepiness. Furthermore, importantly, we found that both depressive and anxiety symptoms in early pregnancy were related to an increase of sleep disturbances throughout the pregnancy.

Our study adds to the literature because previous studies are mainly cross-sectional [4–9] and the studies with longitudinal study design are sparse [10–13]. We confirmed the results gained in previous studies [11–13], as well as the results of our pilot study with 78 pregnant women [10], showing an increase in sleep disturbances towards the end of pregnancy. Using the same sleep questionnaire as in our study, Hedman et al. reported in their longitudinal study of 325 pregnant women that sleep quality declined and insomnia increased as pregnancy proceeded [11]. Similarly, Roman-Galves et al. reported in their longitudinal study of 402 women that insomnia scores measured by the Athens Insomnia Scale increased during pregnancy [12]. Our large study therefore confirmed the findings in previous smaller studies showing that insomnia is a highly frequent symptom during pregnancy and increases towards late pregnancy. Self-reported reasons for sleep disturbances in our study included nocturia, nausea, vomitus, leg cramps, restless legs, joint pain, backaches, heartburn, uncomfortable or unusual sleeping position, nasal congestion, thermoregulatory

problems (too hot/too cold), anxiety, worries, dreams and nightmares, in line with previous studies [5–7]. These symptoms have also been found to increase during the course of pregnancy [6], giving one explanation for the concurrent increase of sleep disturbances.

As for nocturnal breathing problems, in our study, snoring increased along the pregnancy, but witnessed apneas, which were rare, did not increase. Our results confirmed the previous findings [11][15], proposing that nocturnal breathing problems during pregnancy are more often due to flow limitations typical for partial upper airway obstruction, causing snoring [43]. Instead, frank obstructive apnea episodes are rare during pregnancy [43], several factors may impair nocturnal breathing, such as gestational weight gain and estrogen-induced increases in mucosal edema, hyperemia and mucus hypersecretion, which typically narrow upper airways [4].

Contrary to our hypothesis, sleepiness did not increase as pregnancy proceeded. It rather decreased in mid-pregnancy, presumably indicating an effective coping mechanism to deal with any increase in insomnia symptoms. For instance, progesterone, which is considerably increased during pregnancy, has somnolent properties [44]. Further, during pregnancy, secretion of several sleep regulating hormones, such as cortisol, prolactin, melatonin and growth hormone, increases, which may counteract the effect of insomnia symptoms [45]. In addition, sleepiness in different trimesters may stem from different reasons, both physical and mental, which could explain why sleepiness did not exhibit a constant increase in frequency. Similar to our results, in a cross-sectional study with 871 women, Neau and Texier found that sleepiness, evaluated by the Epworth Sleepiness Scale (ESS), was worst in the first trimester and decreased thereafter during pregnancy [6]. In addition, they

also found, as in the above mentioned study by Román-Gálves et al., a U-shape daytime sleepiness similar to our observation, confirming the lower occurrence of sleepiness in mid-pregnancy [12]. In contrast, Mindell et al. showed in their cross-sectional study of 2427 women a high frequency of sleepiness (49%), with no differences occurring during pregnancy [5]. They used the ESS and enrolled the women via a pregnancy-related internet site, possibly leading to over-representation of women with sleepiness symptoms.

We confirmed that both depressive and anxiety symptoms are important for sleep quality during pregnancy. Okun et al. reported results partly similar to ours using three similar measurement point settings during pregnancy in 240 women: depressed women had more insomnia and longer sleep latencies at gwk 20 than non-depressed and also longer sleep latency at gwk 30 and in gwk 36 [28]. Qiu et al. showed in a cross-sectional cohort of 1332 women using one assessment point between gwk 8–19 that women having a mood or anxiety disorder were more likely to report short sleep duration (≤ 6 hours) in early pregnancy [46]. In Qiu et al.'s study, in contrast to our results, no difference in daytime sleepiness was found between the women with prior mood or anxiety disorder compared to those with no such history [46]. Goyal et al., also using only one measurement point in 124 women, reported that depressed pregnant women had more sleep disturbances in late pregnancy than non-depressed [29]. In a recent study of 3645 women by Yu et al., where sleep was assessed with two questions prospectively in three trimesters, it was found that women with a shorter sleep duration (< 8 h/day) and lower sleep quality were at a higher risk for symptoms of depression and anxiety [34]. Additionally, Dorheim et al. reported in a study of 2816 women that depressive symptoms were strongly

associated with insomnia in late pregnancy [31]. However, the present literature cannot give the directions for causality, probably partly because the underlying mechanisms are unclear and certainly multifactorial. In addition to these associations, changes in insomnia and sleepiness symptoms could also be related to changes in depression and anxiety levels. Further studies are needed to evaluate their interrelations.

The strength of our study was the large and encompassing sample with a relatively high response rate. By assessing various insomnia symptoms in a longitudinal study setting, we were able to provide their prevalence rates at all three trimesters and to evaluate the changes in their prevalence during pregnancy. However, as we wanted to assess changes in sleep quality across the pregnancy, responses at all three time points were required. This led to a response rate of 57.3% in our study, which fell in the range in previous studies of 45.3% [34] and 82.9% [12]; thus, our response rate was representative and comparable to other studies. One limitation was that the pre-pregnancy quality of sleep or mood symptoms were not measured. Therefore, we were not able to study whether insomnia and sleepiness symptoms were triggered by pregnancy, and moreover, whether depressive and anxiety symptoms at the beginning of pregnancy were caused by possible pre-pregnancy mood or sleep disturbances.

There are both pros and cons for utilizing self-report questionnaires in data gathering. Firstly, this method likely helped to gather a large sample size and also made it easy for the women to participate. Secondly, the questionnaires that we used are widely used in several different contexts and recognized as suitable tools to evaluate sleep [37], depressive symptoms [39,40] and anxiety symptoms [41,42]. Furthermore, we used a detailed sleep questionnaire, which allowed us to distinguish

between various insomnia and sleepiness symptoms. However, no objectively measured sleep data were collected. The mismatch between subjectively and objectively measured sleep is acknowledged. One important reason for this mismatch is the different time frame in evaluation: in questionnaires like in our study, sleep quality was assessed during the past month, whereas when using objective measurements like polysomnography, sleep quality is measured during only one, or at the most some nights. Also, conducting polysomnography measurements in such a large study as ours would not have been feasible regarding laboratory resources, time consumption and cost-effectiveness. In addition, there are studies showing that subjective perception of sleep is a stronger predictor of mood symptoms than actigraphy-assessed sleep [47,48]. These findings encourage the use of subjective estimation of sleep quality and quantity, although it might be prone to a report bias, both under- and overestimation of disturbances, that we were not able to control. The problem of underestimation is especially pronounced in reporting of snoring and witnessed apneas, which are partly dependent on reporting by the partner or other persons in the household. Nevertheless, the report errors were similar and equivalent for all of the women. As for evaluation of sleepiness, we utilized three questions derived from the BNSQ, instead of more accurate and longer questionnaires like the Epworth sleepiness scale [49], which could partly dilute our findings concerning the frequency of sleepiness.

5. Conclusion

Insomnia symptoms were highly prevalent throughout pregnancy, and insomnia score and all studied insomnia symptoms, such as difficulty falling asleep, nocturnal awakenings per week, frequency of nocturnal awakenings per night and

waking up too early in the morning without the ability to go back to sleep, increased during the course of pregnancy. However, sleepiness did not increase; in fact, it was more common in early pregnancy, and especially morning sleepiness decreased along pregnancy. Depressive and anxiety symptoms that appeared already in early pregnancy interacted with insomnia and sleepiness symptoms throughout pregnancy and thus their detection and care by healthcare professionals taking care of pregnant women are crucial from an early stage in pregnancy. In addition, further studies are needed to evaluate whether mothers with insomnia symptoms but lower sleepiness are less prone to the negative effects of insomnia during pregnancy.

Acknowledgements

We would like to thank all the families that participated in the FinnBrain birth-cohort. The study was financially supported by Turku University Hospital (EVO grant, L.A, P.P-K, L.K.), Academy of Finland, Jane and Aatos Erkko Foundation, Signe and Ane Gyllenberg Foundation (H.K.) and Foundation for Pediatric Research (E.J.P)

References

- [1] Chang JJ, Pien GW, Duntley SP, Macones GA. Sleep deprivation during pregnancy and maternal and fetal outcomes: Is there a relationship? *Sleep Med Rev* 2010;14:107–14. <https://doi.org/10.1016/j.smrv.2009.05.001>.
- [2] Palagini L, Gemignani A, Banti S, Manconi M, Mauri M, Riemann D. Chronic sleep loss during pregnancy as a determinant of stress: Impact on pregnancy outcome. *Sleep Med* 2014;15:853–9. <https://doi.org/10.1016/j.sleep.2014.02.013>.
- [3] Pamidi S, Pinto LM, Marc I, Benedetti A, Schwartzman K, Kimoff RJ. Maternal sleep-disordered breathing and adverse pregnancy outcomes: A systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;210:52.e1-52.e14. <https://doi.org/10.1016/j.ajog.2013.07.033>.
- [4] Mindell J a, Jacobson BJ. Sleep disturbances during pregnancy. *J Obstet Gynecol Neonatal Nurs* 2000;29:590–7.
- [5] Mindell JA, Cook RA, Nikolovski J. Sleep patterns and sleep disturbances across pregnancy. *Sleep Med* 2015;16:483–8. <https://doi.org/10.1016/j.sleep.2014.12.006>.
- [6] Neau J, Texier B. Sleep and Vigilance Disorders in pregnancy. *Eur Neurol* 2009;05:23–9. <https://doi.org/10.1159/000215877>.
- [7] Wilson DL, Barnes M, Ellett L, Permezel M, Jackson M, Crowe SF. Decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals in late pregnancy. *Aust N Z J Obstet Gynaecol* 2011;51:38–46. <https://doi.org/10.1111/j.1479-828X.2010.01252.x>.
- [8] Kizilirmak A, Timur S, Kartal B. Insomnia in pregnancy and factors related to insomnia. *Sci World J* 2012;2012. <https://doi.org/10.1100/2012/197093>.

- [9] Juulia Paavonen E, Saarenpää-Heikkilä O, Pölkki P, Kylliäinen A, Porkka-Heiskanen T, Paunio T. Maternal and paternal sleep during pregnancy in the Child-sleep birth cohort. *Sleep Med* 2017;29:47–56. <https://doi.org/10.1016/j.sleep.2016.09.011>.
- [10] Polo-Kantola P, Aukia L, Karlsson H, Karlsson L, Paavonen EJ. Sleep quality during pregnancy: associations with depressive and anxiety symptoms. *Acta Obstet Gynecol Scand* 2017;96:198–206. <https://doi.org/10.1111/aogs.13056>.
- [11] Hedman C, Pohjasvaara T, Tolonen U, Suhonen-Malm A, Myllylä V. Effects of pregnancy on mothers' sleep. *Sleep Med* 2002;3:37–42.
- [12] Román-Gálvez RM, Amezcua-Prieto C, Salcedo-Bellido I, Martínez-Galiano JM, Khan KS, Bueno-Cavanillas A. Factors associated with insomnia in pregnancy: A prospective Cohort Study. *Eur J Obstet Gynecol Reprod Biol* 2018;221:70–5. <https://doi.org/https://doi.org/10.1016/j.ejogrb.2017.12.007>.
- [13] Facco FL, Kramer J, Ho KH, Zee PC, Grobman WA. Sleep Disturbances in Pregnancy. *Obstet Gynecol Surv* 2010;65:220–2. <https://doi.org/10.1097/01.ogx.0000371710.47597.7a>.
- [14] Izci B, Vennelle M, Liston WA, Dundas KC, Calder AA, Douglas NJ. Sleep-disordered breathing and upper airway size in pregnancy and post-partum. *Eur Respir J* 2006;27:321–7. <https://doi.org/10.1183/09031936.06.00148204>.
- [15] Sarberg M, Svanborg E, Wiréhn AB, Josefsson A. Snoring during pregnancy and its relation to sleepiness and pregnancy outcome - a prospective study. *BMC Pregnancy Childbirth* 2014;14:1–7. <https://doi.org/10.1186/1471-2393-14-15>.
- [16] Reutrakul S, Zaidi N, Wroblewski K, Kay HH, Ismail M, Ehrmann D a, et al. Interactions Between Pregnancy, Obstructive Sleep Apnea, and Gestational

- Diabetes Mellitus. *J Clin Endocrinol Metab* 2013;98:4195–202.
<https://doi.org/10.1210/jc.2013-2348>.
- [17] Maasilta P, Bachour a., Teramo K, Polo O, Laitinen L a. Sleep-related disordered breathing during pregnancy in obese women. *Chest* 2001;120:1448–54. <https://doi.org/10.1378/chest.120.5.1448>.
- [18] Pien GW, Pack AI, Jackson N, Maislin G, Macones G a, Schwab RJ. Risk factors for sleep-disordered breathing in pregnancy. *Thorax* 2014;69:371–7. <https://doi.org/10.1136/thoraxjnl-2012-202718>.
- [19] Alhola P, Polo-Kantola P. Sleep deprivation: Impact on cognitive performance. *Neuropsychiatr Dis Treat* 2007;3:553–67.
- [20] Carter JR, Grimaldi D, Fonkoue IT, Medalie L, Mokhlesi B, Van Cauter E. Assessment of sympathetic neural activity in chronic insomnia: evidence for elevated cardiovascular risk. *Sleep* 2018;41. <https://doi.org/10.1093/sleep/zsy126>.
- [21] Deng HB, Tam T, Chung-Ying Zee B, Yat-Nork Chung R, Su X, Jin L, et al. Short sleep duration increases metabolic impact in healthy adults: A population-based cohort study. *Sleep* 2017;40. <https://doi.org/10.1093/sleep/zsx130>.
- [22] Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? *JAMA* 1989;262:1479–84.
- [23] Leung PL, Hui DSC, Leung TN, Yuen PM, Lau TK. Sleep disturbances in Chinese pregnant women. *BJOG An Int J Obstet Gynaecol* 2005;112:1568–71. <https://doi.org/10.1111/j.1471-0528.2005.00737.x>.
- [24] Steiner M. Perinatal mood disorders: position paper. *Psychopharmacol Bull*

- 1998;34:301–6.
- [25] Dennis CL, Falah-Hassani K, Shiri R. Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *Br J Psychiatry* 2017;210:315–23. <https://doi.org/10.1192/bjp.bp.116.187179>.
- [26] Woody CA, Ferrari AJ, Siskind DJ, Whiteford HA, Harris MG. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. *J Affect Disord* 2017;219:86–92. <https://doi.org/10.1016/j.jad.2017.05.003>.
- [27] Rumble ME, White KH, Benca RM. Sleep Disturbances in Mood Disorders. *Psychiatr Clin North Am* 2015;38:743–59. <https://doi.org/10.1016/j.psc.2015.07.006>.
- [28] Okun ML, Kiewra K, Luther JF, Wisniewski SR, Wisner KL. Sleep disturbances in depressed and nondepressed pregnant women. *Depress Anxiety* 2011;28:676–85. <https://doi.org/10.1002/da.20828>.
- [29] Goyal D, Gay CL, Lee KA. Patterns of sleep disruption and depressive symptoms in new mothers. *J Perinat Neonatal Nurs* 2007;21:123–9. <https://doi.org/10.1097/01.JPN.0000270629.58746.96>.
- [30] Field T, Diego M, Hernandez-Reif M, Figueiredo B, Schanberg S, Kuhn C. Sleep disturbances in depressed pregnant women and their newborns. *Infant Behav Dev* 2007;30:127–33. <https://doi.org/10.1016/j.infbeh.2006.08.002>.
- [31] Dørheim SK, Bjorvatn B, Eberhard-Gran M. Insomnia and Depressive Symptoms in Late Pregnancy: A Population-Based Study. *Behav Sleep Med* 2012;10:152–66. <https://doi.org/10.1080/15402002.2012.660588>.
- [32] Swanson LM, Pickett SM, Flynn H, Armitage R. Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking

- mental health treatment. *J Womens Health (Larchmt)* 2011;20:553–8.
<https://doi.org/10.1089/jwh.2010.2371>.
- [33] Skouteris H, Germano C, Wertheim EH, Paxton SJ, Milgrom J. Sleep quality and depression during pregnancy: a prospective study. *J Sleep Res* 2008;17:217–20. <https://doi.org/10.1111/j.1365-2869.2008.00655.x>.
- [34] Yu Y, Li M, Pu L, Wang S, Wu J, Ruan L, et al. Sleep was associated with depression and anxiety status during pregnancy: a prospective longitudinal study. *Arch Womens Ment Heal* 2017;20:695–701.
<https://doi.org/10.1007/s00737-017-0754-5>.
- [35] Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and elaboration. *Int J Surg* 2014;12:1500–24. <https://doi.org/10.1016/j.ijsu.2014.07.014>.
- [36] Karlsson L, Tolvanen M, Scheinin NM, Uusitupa HM, Korja R, Ekholm E, et al. Cohort Profile: The FinnBrain Birth Cohort Study (FinnBrain). *Int J Epidemiol* 2018;47:15–16j. <https://doi.org/10.1093/ije/dyx173>.
- [37] Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J Sleep Res* 1995;4:150–5.
<https://doi.org/10.1111/j.1365-2869.1995.tb00205.x>.
- [38] Unettomuus. Käypä hoito -suositus: Suomalaisen Lääkäriseuran Duodecimin ja Suomen Unitutkimusseura ry:n asettama työryhmä. Helsinki: Suomalainen Lääkäriseura Duodecim 2017 (päivitetty 20.2.2020). www.kaypahoito.fi)
- [39] Gibson J, McKenzie-McHarg K, Shakespeare J, Price J, Gray R. A systematic review of studies validating the Edinburgh Postnatal Depression Scale in antepartum and postpartum women. *Acta Psychiatr Scand* 2009;119:350–64.

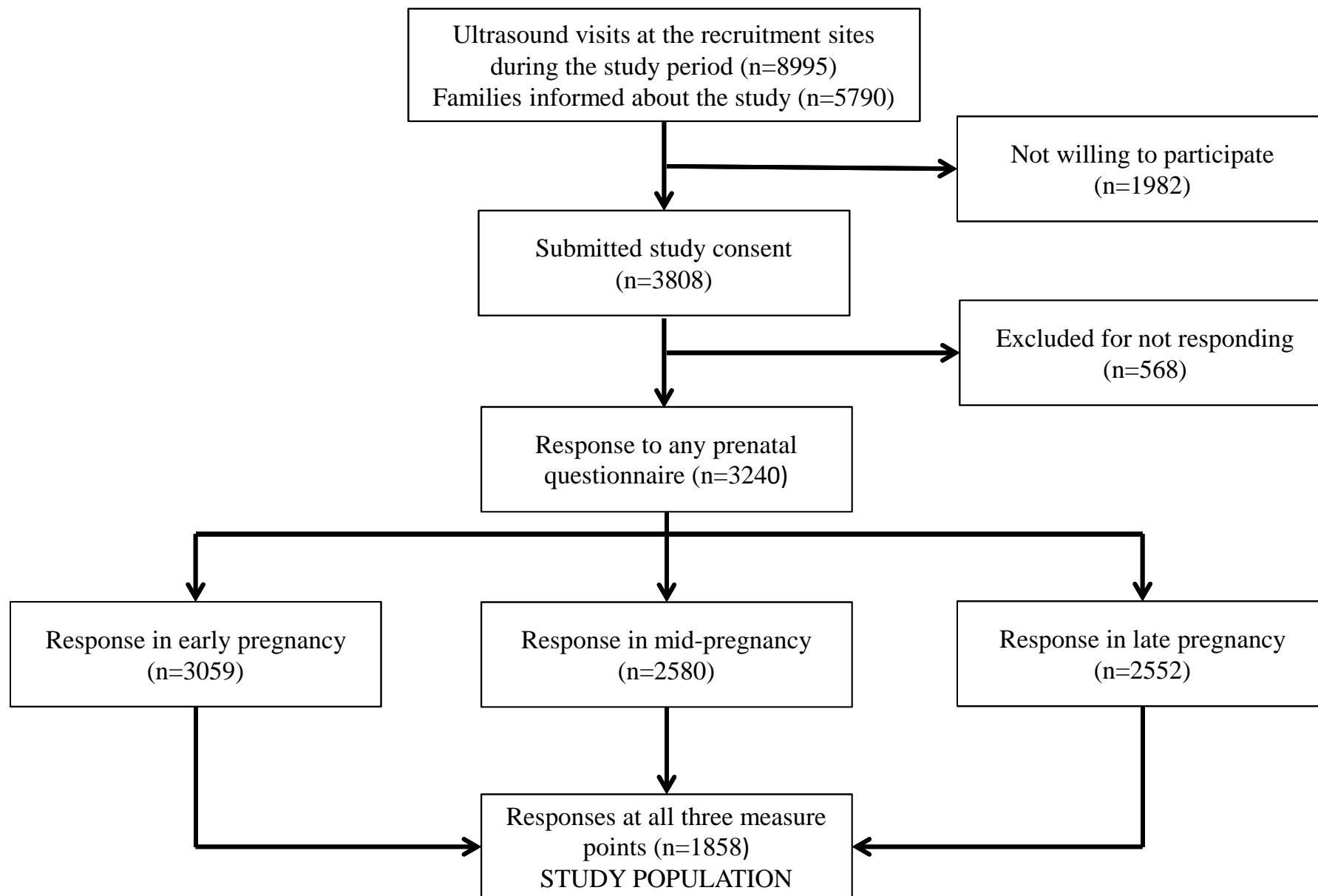
- <https://doi.org/10.1111/j.1600-0447.2009.01363.x>.
- [40] Rubertsson C, Börjesson K, Berglund A, Josefsson A, Sydsjö G. The Swedish validation of Edinburgh Postnatal Depression Scale (EPDS) during pregnancy. *Nord J Psychiatry* 2011;65:414–8. <https://doi.org/10.3109/08039488.2011.590606>.
- [41] Derogatis LR, Lipman RS, Covi L. SCL-90: an outpatient psychiatric rating scale--preliminary report. *Psychopharmacol Bull* 1973;9:13–28.
- [42] Holi MM, Sammallahti PR, Aalberg VA. A Finnish validation study of the SCL-90. *Acta Psychiatr Scand* 1998;97:42–6. <https://doi.org/10.1111/j.1600-0447.1998.tb09961.x>.
- [43] Bourjeily G, Fung JY, Sharkey KM, Walia P, Kao M, Moore R, et al. Airflow limitations in pregnant women suspected of sleep-disordered breathing. *Sleep Med* 2014;15:550–5. <https://doi.org/10.1016/j.sleep.2014.01.004>.
- [44] Lancel M, Faulhaber J, Holsboer F, Rupprecht R. Progesterone induces changes in sleep comparable to those of agonistic GABAA receptor modulators. *Am J Physiol* 1996;271:E763-72.
- [45] Balserak BI, Lee K. Sleep Disturbances and Sleep-Related Disorders in Pregnancy. *Princ. Pract. Sleep Med. Fifth Ed.*, 2010, p. 1572–86. <https://doi.org/10.1016/B978-1-4160-6645-3.00138-9>.
- [46] Qiu C, Gelaye B, Fida N, Williams MA. Short sleep duration, complaints of vital exhaustion and perceived stress are prevalent among pregnant women with mood and anxiety disorders. *BMC Pregnancy Childbirth* 2012;12. <https://doi.org/10.1186/1471-2393-12-104>.
- [47] Bei B, Milgrom J, Ericksen J, Trinder J. Subjective Perception of Sleep, but not its Objective Quality, is Associated with Immediate Postpartum Mood

Disturbances in Healthy Women. *Sleep* 2010;33:531–8.

<https://doi.org/10.1093/sleep/33.4.531>.

- [48] Park EM, Meltzer-Brody S, Stickgold R. Poor sleep maintenance and subjective sleep quality are associated with postpartum maternal depression symptom severity. *Arch Womens Ment Health* 2013;16:539–47. <https://doi.org/10.1007/s00737-013-0356-9>.

- [49] Johns MW. Sleepiness in Different Situations Measured by the Epworth Sleepiness Scale. *Sleep* vol. 17. 1994.



Highlights:

- General sleep quality declined as pregnancy proceeded
- Various insomnia symptoms were highly prevalent and increased during pregnancy
- Sleepiness did not increase but rather decreased during second trimester
- Depressive and anxiety symptoms were associated with sleep disturbances

Contributions

Linda Aukia (ORCID iD 0000-0003-1930-2984) is the principal investigator and writer of the paper and co-leader of the present sub-study. Tuire Jänkälä (ORCID iD 0000-0003-0580-1213), Mimmi Tolvanen, Riikka Korja (ORCID iD 0000-0002-6833-1565) and Linnea Karlsson (ORCID iD 0000-0002-4725-0176) are co-investigators and co-writers. Hasse Karlsson (ORCID iD 0000-0002-4992-1893) is the leader of the FinnBrain study, co-investigator and co-writer. E.Juulia Paavonen (ORCID iD 0000-0002-1421-9877) and Päivi Polo-Kantola (ORCID iD 0000-0003-0665-0306) are co-leaders of the present sub-study, co-investigators and co-writers.

Journal Pre-proof